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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| SLOBODYANSKY, ELIZABETH | |
| ART UNIT | PAPER NUMBER |
| 1652 | |

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/912,559 | ROEMISCH ET AL. | |
| | Examiner | Art Unit | |
| | Elizabeth Slobodyansky | 1652 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *13 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *3-29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *7,10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

The preliminary amendment filed concurrently with the application on July 26, 2001 amending the specification to correct clerical errors has been entered.

Claims 1-29 are pending.

### *Election/Restriction*

Applicant's election with traverse of Group I, claims 1 and 2, in Paper No. 13 filed November 13, 2002 is acknowledged. The traversal is on the ground(s) that "the search and examination of the entire application can be made without serious burden" (page 2, 1st paragraph). And further, "at minimum, Group I is drawn to polynucleotide sequences that include those encoding the polypeptide sequences of Group II. ... a thorough search for the subject matter any one of these groups should involve the subject matter of the other" (page 2, 2nd paragraph). This is not found persuasive because Inventions I and II are patentably distinct because a DNA and a polypeptide are different compounds each with its own chemical structure and function, and they have different utilities. A DNA molecule of invention I can be used for the production of a polypeptide of invention II and as a hybridization probe. A polypeptide of invention II can be obtained by a materially different method such as by the biochemical purification or chemical synthesis.

Applicants further argue issues related to non-elected Groups (page 2). They will be address when these Groups will be examined.

The requirement is still deemed proper and is therefore made FINAL.

As noted by Applicants, claims 18-22 inadvertently have not been placed into any particular group and Applicants "suggest that these claims be placed in either Group V or Group XII" (page 1). Invention of Group II and claims 18-22 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case a polypeptide of invention II can be used for the screening for protease modulators, for the production of antibodies and in a process of claims 18-22.

Claims 3-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups III-XII, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 13.

***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### *Specification*

The disclosure is objected to because "AVENTIS BEHRING GMBH 2000/A008-A7" should be deleted from the abstract.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to "a mutant of the nucleotide sequence coding for the factor VII-activating protease (FSAP), comprising at least one of [mutations]". Since "comprising" is open language, claim 1 reads on a mutant comprising any number of mutations in addition to the two specific mutations (1177 and/or 1601).This amounts to any nucleotide structure that is not necessarily homologous to SEQ ID NO:1.Thus, the claim is drawn to an enormous genus of FSAP mutants.

Applicants disclose a single species of said genus, SEQ ID NO:2, that differs from the wild type SEQ ID NO:1 by a G to C base exchange at nucleotide position 1177

and a G to A base exchange at nucleotide position 1601. Moreover, the specification fails to describe any other identifying characteristics or properties of mutant FSAPs other than the "functionality" of encoding "FSAP" and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO:2 that differs from SEQ ID NO:1 by two mutations at positions 1177 and 1601, does not reasonably provide enablement for a mutant of the nucleotide sequence coding for the factor VII-activating protease (FSAP), comprising at least one of the two mutations at positions 1177 and 1601 and having unknown homology to SEQ ID NO:1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of

direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The scope of the claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of FSAP mutants broadly encompassed by the claim. Since the amino acid/nucleotide sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequence of a single mutant having the nucleotide sequence of SEQ ID NO:2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the

desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass mutant FSAPs with unknown homology to SEQ ID NO:1 and having the requisite properties or any properties because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting FSAP activity; (B) the general tolerance of FSAP to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any FSAP residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of modifications in SEQ ID NO:1.

Without such guidance, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 refers to the base exchange at the specific positions of "the nucleotide sequence coding for the factor VII-activating protease (FSAP)".The sequence of FSAP is not invariant among species. Furthermore, allelic variations and splicing variants of human proteins are very common. Knowing the sequence is necessary to determine the position of the claimed mutation and therefore, to define the metes and bounds of the claim. Amending the claim to refer to SEQ ID NO:1 would obviate this rejection.

### ***Allowable Subject Matter***

Claim 2 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kitamura (GenBank accession D49742) teach a 3008 nucleotide sequence, nucleotides 97-1779 of which are 100% identical to SEQ ID NO:1 of the instant invention and therefore, comprise SEQ ID NO:1.

Romisch et al. (US Patent 6,528,299) teach protease for activating clotting Factor VII comprising SEQID NO:1 (claim 2). SEQ ID NO:1 is 1005 identical to residues 314-324 of SEQ ID NO:3 of the instant invention. Thus, this protease appears to be FSAP of the instant invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

March 7, 2003